REMARKS

I. Status of the Claims

Claims 4, 6-8, 17, 20-28, and 48 are pending in the application following entry of this amendment. Claim 48 has been amended. Since the amendment obviates the outstanding grounds of rejection as discussed below, reduces the number of issues, contains no new matter, and places the application in condition for allowance or better condition for appeal, the amendment should be entered.

Claims 4, 6-8, 17, 20-28 and 48 are rejected under 35 U.S.C. § 112, first paragraph as failing to comply with the enablement requirement. Claim 48 is objected to as being dependent upon a cancelled base claim.

II. Claim objection

Claim 48 was objected to as being dependent upon a cancelled base claim. Claim 48 has been amended to depend from claim 6.

III. The claims are patentable under 35 U.S.C. § 112, paragraph 1

Claims 4, 6-8, 17, 20-28 and 48 were rejected under 35 U.S.C. § 112, first paragraph, for allegedly containing non-enabled subject matter. The Examiner alleges that the specification, while being enabling for a recombinant nucleic acid molecule consisting of a nucleotide sequence encoding hepatitis C virus nonstructural proteins NS3, NS4 and NS5, wherein said nucleotide sequence is operably linked to regulatory elements, said regulatory elements comprising a promoter, enhancer, polyadenylation sequence, and at most the 9 most 3' nucleotides of the 5'UTR of a hepatitis C virus, does not reasonably provide enablement for a recombinant nucleic acid molecule consisting of a nucleotide sequence encoding hepatitis C virus nonstructural proteins NS3, NS4 and NS5, wherein said nucleotide sequence is operably linked to regulatory elements, said regulatory elements comprising a promoter, enhancer, polyadenylation sequence, and a 5' untranslated region from any gene. Applicants traverse the rejection.

Applicants' claimed invention is a recombinant nucleic acid molecule consisting of a nucleotide sequence encoding hepatitis C virus nonstructural proteins NS3, NS4 and NS5,

wherein said nucleotide sequence is operably linked to regulatory elements, said regulatory elements comprising a promoter, enhancer, polyadenylation sequence, and a hepatitis C virus 5'-UTR. Furthermore, the claimed invention is a method of inducing an immune response against hepatitis C virus in a human uninfected by hepatitis C virus comprising administering the recombinant nucleic acid molecule. Contrary to the Examiner's rejection, the specification does enable a person skilled in the art to practice the claimed invention, in part, wherein the regulatory elements comprise a hepatitis C virus 5'-UTR. The specification is enabling for regulatory elements comprising more than the "9 most 3' nucleotides of the 5'-UTR of a hepatitis C virus." The specification states that the 5'-UTR can include the last 9 nucleotides of the HCV 5'-UTR, the last 50 nucleotides, the last 100 nucleotides, the last 150 nucleotides, the last 200 nucleotides the last 250 nucleotides, the last 300 nucleotides, or the entire HCV 5' UTR. See specification, for example, page 10, line 18 to page 11, line 2. All of these proportionate lengths of HCV 5' UTR are functional in an expression construct comprising a nucleic acid encoding the HCV NS3, NS4, and NS5 genes. The specification, as filed, and publications as of the filing date that are currently of record support the transcriptional activity of expression constructs incorporating the HCV 5' UTR.

Yoo et al., *Virology* **191:** 889-899, 1992 (submitted herein with a supplemental Information Disclosure Statement) further support the enabling disclosure of the specification. The Yoo et al. reference measured transient expression from an expression construct with a chloramphenicol transferase (CAT) reporter and a promoter region including various regions of the HCV 5' UTR. These experiments mapped the *cis*-acting elements controlling translation in the HCV genome linking a full length (nucleotides 1 to 341) or deleted versions of the 5' UTR of HCV RNA to the coding region of CAT mRNA. See, for example, Figure 1 of Yoo et al. The nucleotide sequence of the 5' UTR of HCV RNA corresponds to SEQ ID NO: 2 (nucleotides 1 to 341) in the specification. The Yoo et al. reference identifies "an efficient positive control element that stimulates translation may be present downstream from nucleotide 255. This 86-nucleotide sequence contains a 28-nucleotide sequence at position 291 to 281 with 90% sequence identity... to a PEST-IV [element]." See for example, Yoo et al., paragraph spanning pages 893 to 894 and Figure 3. Therefore, a skilled practitioner would predict that a construct containing regions of the 5'-UTR of HCV, *e.g.*, the PEST-IV element, would produce increased levels of HCV NS3, NS4, or NS5 protein compared to a construct

lacking the 5'UTR of HCV and thus increase the likelihood of producing a protective immune response in a mammal.

As further stated in the Declaration by Dr. Jack Wands in Paper No. 13:

> "Utilizing information provided in the subject application and in Yoo et al. *Virology* **191**: 889-899, 1992, one skilled in the art would understand the function of the 5' UTR of hepatitis C virus, including the positive and negative translational control elements within the 5'-UTR. One skilled in the art would be able to operably link the 5'UTR of hepatitis C virus to a recombinant nucleic acid molecule acting as an expression plasmid for proteins, for example, hepatitis C virus non-structural (NS) protein."

Declaration of Dr. Jack Wands under 37 C.F.R. § 1.132 in Paper No. 13.

The Examiner argues that multiple premature start codons present in the 5'-UTR of the HCV would have a negative effect on the efficiency of translation. Utilizing information provided in the subject application and in the Yoo et al. reference, one skilled in the art would understand the negative effects in the region of ORF1, ORF2, ORF3, and ORF4 within the 5'-UTR of HCV and the positive effects on translation in the region of PESTI-IV within the 5'-UTR of HCV. See for example, Yoo et al. reference, Figure 1. Contrary to the Examiner's assertion, one skilled in the art would be able to operably link the 5'UTR of hepatitis C virus to a recombinant nucleic acid molecule acting as an expression plasmid for proteins, for example, hepatitis C virus non-structural (NS) protein.

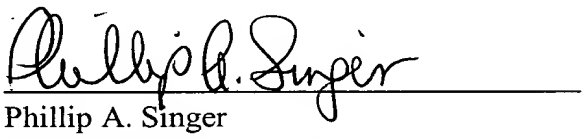
Therefore a person of skill in the art would know how to utilize the HCV 5' UTR to enhance expression of the HCV NS3, NS4, and NS5 proteins. The specification enables one of skill in the art to utilize various regions of the 5' UTR of a hepatitis C virus (*i.e.*, more than "at most the 9 most 3' nucleotides of the 5' UTR of a hepatitis C virus") to construct a recombinant nucleic acid molecule as claimed. Furthermore, the specification enables one of skill in the art to utilize various regions of the 5' UTR of a hepatitis C virus to construct and use the recombinant nucleic acid molecule encoding HCV NS3, NS4, and NS5 in a method of inducing an immune response against hepatitis C virus in a human uninfected by hepatitis C virus. Accordingly, applicants respectfully request that the rejection of claims 4, 6-8, 17, and 20-28 and 48 under 35 U.S.C. § 112, first paragraph, be withdrawn.

IV. Conclusion

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 206-332-1380.

Date: October 27, 2005



Phillip A. Singer
Registration No. 40,176

Woodcock Washburn LLP
One Liberty Place - 46th Floor
Philadelphia PA 19103
Telephone: (215) 568-3100
Facsimile: (215) 568-3439